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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/938,418 | 08/23/2001 | Avi Ashkenazi | P5009R1 | 2589 |

7590 11/04/2004

Attn: Mark T. Kresnak, Ph.D.
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| EXAMINER | |
|---|---|
| SPECTOR, LORRAINE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | |

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/938,418 | ASHKENAZI ET AL. | |
| | Examiner | Art Unit | |
| | Lorraine Spector, Ph.D. | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/15/02, 9/22/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

### *Election/Restrictions*

Applicant's election without traverse of Group III in the reply filed on 8/14/2004 is acknowledged.

### *Information Disclosure Statement*

The information disclosure statement filed 9/22/2003 could not be considered, as no references accompanied the submission.

References 18 and 19 on the IDS submitted 9/14/2004 have not been considered, as insufficient identifying information has been provided on the form USCOMM-DC 80-398.

### *Specification*

The disclosure is objected to because of the following informalities; appropriate correction is required for reach item listed:

The specification includes a list of claims at pages 7-17 which are designated as "additional embodiments", but are phrased as claims. The inclusion of claims in the specification is improper.

The amendment filed 8/14/2001 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Applicants have amended the application to change the cross-reference to related applications, including the incorporation by reference to the newly recited applications. As those applications were not incorporated by reference in this application as originally filed, the incorporation of such applications, which contain substantial information regarding the utility of the claimed antibodies, constitutes new matter. Applicants are reminded that a claim to priority is not the same as an incorporation by reference, and that the blanket incorporation by reference to another application does not obviate the requirements of 35 U.S.C. §101 and 112 that there be a disclosed, enabled utility, *in this application as originally filed.*

Applicant is required to cancel the new matter in the reply to this Office Action.

***Priority***

It is noted that the protein to which the claimed antibodies bind, identified herein as TAT171, but in other applications as PRO866, was shown to induce mouse kidney mesangial cell proliferation and to induce the switch from adult to fetal hemoglobin in PCT US00/04341, which published as WO 00/53756, filed 2/18/00. However, there was no such disclosure in this application as originally filed, hence the new incorporation by reference to that application is improper, as it introduces new matter into the specification.

The sole use for the claimed antibodies disclosed in *this* specification as originally filed is as a cancer diagnostic. The Examiner cannot find such utility disclosed in the applications to which priority is currently claimed; specifically, it is not present in PCT/US00/04341 (WO/00/53756), PCT/US99/05028 (WO99/46281), nor in provisional application 60/081071.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to the date recited above which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to that date.

In view of the above, priority for this application is set at the instant filing date, 8/23/2001.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims that recite "the extracellular domain" of the protein to which the claimed antibodies bind are indefinite as no extracellular domain has been described. Therefore, the metes and bounds of the claims cannot be determined. For example, see Claim 1, parts (c) and (d). Further, if the protein had an extracellular domain, the recitation of "the extracellular domain"..."lacking its associated signal sequence" (claim 1, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell. Finally, the recitation that the polypeptide lacks "its associated signal peptide" is indefinite, as no signal peptide has been described.

Claim 14 is additionally indefinite as it is not clear what effect the further limitation has on the claimed antibody; such might be an inherent property of the antibody, or the cell to which it binds (in which case the claim would be found not to be further limiting), or alternatively, might be intended to invoke a further structural limitation.

The remaining claims are rejected for depending from an indefinite claim.

***Deposit requirement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, and 11-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention (see 37 C.F.R.§1.808(a)). Examiner acknowledges the

deposit of organisms under accession number ATCC 209750 under terms of the Budapest Treaty on International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure in partial compliance with this requirement. However, in order to be fully compliant with the requirement, applicants must state that the deposit will be maintained for a term of at lest 30 years *and at least five (5) years after the most recent request for the furnishing of a sample of the deposit was received by the depository.* See 37 C.F.R.§1.806.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-9 and 12-15 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 6,682,902 (Harkins et al.). The Harkins patent merits priority to the filing date of application 60/172,370, filed 12/16/1999.

Harkins discloses and claims methods that use antibodies to a protein that is identical to SEQ ID NO: 8 of this application at all but 3 amino acids, at positions 38, 122 and 242, as well as antibodies to specific fragments that are identical to the corresponding portions of SEQ ID NO: 8; see claims 1 and 4-7. Monoclonal and polyclonal antibodies are included, as well as labeled antibodies. Conjugation to cytotoxic agents is disclosed at col. 28, lines 11-15. Chimeric and humanized antibodies are disclosed at column 26.

Claims 1-8 and 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by WO99/46281 (Wood et al., cited by applicants) .

Wood et al. teaches a polypeptide that is 100% identical to SEQ ID NO:8. Antibodies to the protein are taught for example at pages 135-137, including monoclonal, polyclonal and humanized, which are found at page 196. Though Wood does not specifically disclose production of antibodies in bacteria or CHO cells, the limitations of claims 12 and 13 do not affect the nature of the antibodies so produced, which are therefore anticipated by those of Wood. Coupling of antibodies to detectable markers is disclosed at page 198. As the detectable markers include radioactive isotopes, the limitations of claims 6-8 are inherently met.

Claims 1-9 and 21-15 are rejected under 35 U.S.C. 102(b) as being anticipated by WO00/37638 (Ashkenazi et al., cited by applicants). Ashkenazi et al. teaches a polypeptide that is 100% identical to SEQ ID NO: 8. At page 8 they teach recombinantly produced antibodies produced in bacteria or yeast, as well as monoclonal, fragment, chimeric, humanized and conjugated antibodies. See also claims 37-38. At pages 65-67, antibodies are discussed in further detail, including linkage of such to toxin molecules. Accordingly, the claims are anticipated by Ashkenazi et al.

Claims 1-9 and 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by WO98/45442 (Sheppard et al., cited by applicants). Sheppard et al. teaches a polypeptide that is 100% identical to SEQ ID NO: 8. Labeled antibodies are disclosed at pages 33-34, for example. At page 68-71 they teach monoclonal, fragment, chimeric, humanized and conjugated antibodies, including linkage of such to toxin molecules. Accordingly, the claims are anticipated by Sheppard et al.

Claims 1-8 and 12-15 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,871,969 (Hastings et al., cited by applicants). The Hastings patent merits priority to at least 2/12/1997.

Hastings discloses a protein designated human neuronal attachment factor-1 (NAF-1), which is 98.9% identical to SEQ ID NO: 8. Monoclonal and polyclonal antibodies are included, as well as labeled antibodies, at col. 24-26. Chimeric and humanized antibodies are also disclosed at column 26. Though Hastings does not specifically disclose production of antibodies in bacteria or CHO cells, the limitations of claims 12 and 13 do not affect the nature of the antibodies so produced, which are therefore anticipated by those of Hastings.

Claims 1-8 and 12-15 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 6,287,777 (Sytkowski et al., cited by applicants). The Sytkowski patent merits priority to at least 8/10/1999.

Sytkowski discloses gene designated NPG-1, that is differentially expressed in prostate tumors (title). The encoded protein is 88.9% identical to SEQ ID NO: 8, and is 100% identical at residues 1-144. Monoclonal and polyclonal antibodies are included, as well as labeled antibodies, at col. 26-29. Chimeric and humanized antibodies are also disclosed therein. Though Sytkowski does not specifically disclose production of antibodies in bacteria or CHO cells, the limitations of claims 12 and 13 do not affect the nature of the antibodies so produced, which are therefore anticipated by those of Sytkowski. As the detectable markers include radioactive isotopes, the limitations of claims 6-8 are inherently met.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harkins or Ashkenazi or Sheppard, any one in view of U.S. Patent Number 5,208,020 (Chari et al.).

Claims 10 and 11 contain the limitation that the toxin to which the claimed antibody is conjugated is a maytansinoid, or calicheamicin. Each of the primary references teach the claimed antibodies conjugated to a toxin, but do not specifically teach either of these two toxins.

Chari et al. disclose and claim a cytotoxic agent comprising one or more linked to a monoclonal antibody (see, e.g. claim 1). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute maytansinoids as the toxin in the antibody/toxin conjugates of any of the primary references for their known and expected properties, as taught by Chari et al. Accordingly, the invention, taken as a whole, is *prima facie* obvious.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. ***Effective 1/21/2004, Dr. Spector's telephone number is 571-272-0893.***

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Ms. Brenda Brumback, at telephone number 571-272-0961.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lorraine Spector, Ph.D.
Primary Examiner

10-28-04